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| EXAMINER | |
|---|---|
| RAMACHANDRAN, UMAMAHESWARI | |
| ART UNIT | PAPER NUMBER |
| 1627 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/565,713 | SCHELLER ET AL. | |
| | Examiner | Art Unit | |
| | UMA RAMACHANDRAN | 1627 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *16,17,24-55,57,58,60,62,64 and 68-78* is/are pending in the application.

4a) Of the above claim(s) *16,36 and 68-77* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,24-35,37-55,57,58,60,62,64 and 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/8/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/8/2010 has been entered. Claims 1-15, 18-23, 56, 59, 61, 63, 65-67 have been cancelled. Claims 16, 36, 68-77 are withdrawn from consideration. Claims 35, 58, 60, 62 and 64 have been amended. Claims 16, 17, 24-55, 57, 58, 60, 62, 64, 68-78 are pending. Claims 17, 24-35, 37-55, 57, 58, 60, 62, 64, 78 are examined based on the merits herein.

### *Application Priority*

This application is a U.S. national stage filing under 35 U.S.C. §371 of International Application No. PCT/EP2004/008169 filed on July 22, 2004, which claims priority of German Application No. DE 103 34 187.0 filed on July 26, 2003.

### *Information Disclosure Statement*

The information disclosure statement (IDS) filed on 1/28/2008 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the IDS is being considered by the Examiner.

### *Response to Remarks/Arguments*

Applicants' arguments regarding the 112(1) rejection have been fully considered. Applicants' amendments, arguments and further consideration necessitated the

withdrawal of 112(1) rejection. Applicants' arguments regarding the ODP rejection have been fully considered and found not to be persuasive. Applicants' state that "The rejection is provisional because the allegedly conflicting claims have not yet been patented. Applicant may elect to argue to overcome this ground of rejection or to provide a terminal disclaimer (to the extent necessary) once the present claims have been found to be otherwise allowable and/or once the '699 application issues as a patent". A modified ODP rejection is made and is given below for Applicants' convenience. Applicants' arguments regarding the 103(a) rejection have been fully considered but are moot in view of the new grounds of rejection. Any rejection of record not addressed herein is withdrawn. Further search and consideration necessitated the new 103 rejections presented in this office action.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 17-35, 37-67 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13-20, 24-47, 60-71, 83 of copending Application No. 10/565,699. Although the conflicting claims are not identical, they are not patentably distinct from each other because both teach a method of treating depression comprising administering rotigotine. Claims 17-25, 37-67 of the instant application teach a method of treating depression comprising administering 5,6,7,8-tetrahydro-6- [propyl- [2-(2-thienyl)ethyl] amino]- 1-naphthol or a physiologically acceptable salt thereof that includes the s-isomer rotigotine (elected species) and additional drugs that include antidepressants, antipsychotics, anxiolytics, anti-migraine and sedatives. Claims 13-20, 24-47, 60-71, 83 of the co-pending application '699 teach a method of treating depression comprising administering rotigotine and additional drugs that include antidepressants, antipsychotics, anxiolytics, anti-migraine and sedatives.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 17, 30, 37, 51-55 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 5, 18, 23, 24, 27 and 28 of copending Application No. 11/060,997. Claims 17, 30, 37, 51-55 of the instant application teaches a method of treating depression comprising administering 5,6,7,8-tetrahydro-6- [propyl- [2-(2-thienyl)ethyl] amino]- 1-naphthol or a physiologically

acceptable salt thereof that includes the s-isomer rotigotine (elected species), transdermal administration of the compound at a dosage amount of 0.5-50 mg/day. Claims 15, 18, 23, 24, 27 and 28 of the co-pending application ('997) teaches a method for treatment or prophylaxis of dopaminergic cell loss in a subject suffering from or susceptible to a disease associated with increased dopaminergic cell loss, comprising administration of rotigotine, or a salt or prodrug thereof to the subject and wherein the subject has one or more clinical symptoms selected from the group consisting of smell disorder, depression, sleep disorder etc, transdermal administration of the compound at a dosage amount of 0.05-50 mg/day.

It would have been obvious to a person of ordinary skill in the art at the time of the invention to have used ritogotine in treating depression from the claims 5, 18, 23, 24, 27 and 28 of co-pending application '997 because the claims teaches a method for treatment or prophylaxis of dopaminergic cell loss in a subject suffering from or susceptible to a disease associated with increased dopaminergic cell loss, comprising administration of rotigotine, or a salt or prodrug thereof to the subject and wherein the subject has one or more clinical symptoms selected from the group consisting of smell disorder, depression, sleep disorder etc. Thus it would be obvious to a person of ordinary skill in the art that administration of rotigotine is useful in treating a clinical symptom such as depression in a subject.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 17, 24-34, 37-55, 78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nichols et al. (U.S. 4,501,890) in view of Pfeiffer (Drugs Aging, 2002, vol. 19, no. 8, p. 561-570) and (Lauterback et al. (U.S. 2003/0027793).

Nichols et al. teach that the compounds of Formula III and IV are dopamine D2 agonist and are substantially devoid of other agonist or antagonist blocking activities. As D2 agonists, the compounds are useful in treating Parkinson's syndrome and depression in mammals (see abstract and column 3, lines 20-26).

The reference does not teach that rotigotine treats any type of depression (claims 25-28, 38-50) in humans (claim 24) or that rotigotine is administered parenterally, transdermally or mucosally (claim 30). Nichols et al. also does not teach the amounts of rotigotine to be administered (claim 34, 51-55).

Pfeiffer teaches that rotigotine is a known D2 receptor agonist and is a well tolerated candidate for transdermal Parkinson's disease treatment (see page 566, column 2, 3.3 Rotigotine, first paragraph)

Lauterback teaches a silcon based transdermal therapeutic system containing 0.1 to 3.15 mg/cm$^2$ of rotigotine as active ingredient for the treatment of Parkinson's disease (see abstract) wherein said transdermal therapeutic system induces a mean plasma concentration of rotigotine in the range of 0.4 to 2 ng/ml 24 h after administration [0030]. The reference further teaches that rotigotine is a dopamine receptor agonist and psychological disorder such as depression may also accompany Parkinson's disease (para 0002). The reference teaches daily dosages of 4.5, 9.0 and 13.5 and 18 mg patches can be administered (para 0045). The reference teaches silicone-based transdermal therapeutic system with the silicone compound as a pressure sensitive adhesive or a mixture thereof forming a matrix in which the other components of the transdermal system are embedded (para 0017).

A person of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Nichols et al. and the compound rotigotine to treat any type of depression in humans because of the following teachings: 1) Nichols et al. provides the teaching that D2 agonist treat depression and Parkinson's disease; 2) Pfeiffer teaches that rotigotine is a known D2 agonist and well tolerated for transdermal Parkinson's disease in humans; 3) Lauterback teaches ritogotine in treating Parkinson’s disease and further teaches that depression may also accompany Parkinson’s disease. Thus, since it is known that D2 agonist treat both depression and

Parkinson's disease, one skilled in the art would be motivated to try a known effective D2 agonist that treats Parkinson's disease to also treat any type of depression or depression associated with Parkinson's disease. It would have been obvious to one having ordinary skill in the art at the time of the invention to have formulated as an ointment or a plaster having the active ingredient rotigotine for transdermal administration in treating depression because Lauterbach et al. teaches transdermal therapeutic system comprising rotigotine and further teach the dosage amounts for administration to a patient. Accordingly, one having ordinary skill in the art would have been motivated to administer the drug transdermally in the claimed amounts because it has been shown in the prior art that such formulation is possible and the drug dosage claimed is a safe amount. Though Lauterbach et al. do not explicitly teach establishment of substantial constant plasma level of rotigotine upon administration for treating depression the reference teaches a mean plasma concentration of rotigotine in the range of 0.4 to 2 ng/ml 24 h after administration. Also, the pharmaceutical forms, e.g., sustained release, immediate release etc are all deemed obvious since they are all within the knowledge of the skilled pharmacologist and represent conventional formulations. A person of ordinary skill in the art at the time of the invention would have been motivated to have a controlled release of the drug is to eliminate potential under and over dosing, maintain the drug levels within a desired range of concentration, the need for fewer administration and for increased patient compliance. Despite obvious differences in etiology, many of the conditions including Parkinson's, Alzheimer's disease, brain tumor, epilepsy etc share depression as a common clinical symptom.

Depression is a symptom associated with many diseases and the diseases associated with depression or the types of depression is irrelevant if depression can be treated by administration of a drug.

Claims 35 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nichols et al. (U.S. 4,501,890) in view of Pfeiffer (Drugs Aging, 2002, vol. 19, no. 8, p. 561-570) and (Lauterback et al. (U.S. 2003/0027793) as applied to claims 10-15, 17, 30, 32-44 above and in view of Maj (US 6,255,329).

Nichols et al. in view of Pfeiffer and Lauterbach et al. teachings discussed as above.

The references do not teach addition of one or more antidepressants to compound of formula of claim 17 in treating depression.

Maj teaches treatment of depression in patients comprising administering pramipexole and sertraline (see abstract, col. 4, claim 10). Maj teaches that in combination therapy, the agents can be co-administered separately or as components of a single pharmaceutical dosage form and the drugs can be in different dosage forms (col.2. lines 11-30).

It would have been obvious to one having ordinary skill in the art to treat depression comprising administering compound of formula of claim 17, including rotigotine (elected species) along with one or more antidepressant , sertraline (elected species) in treating depression because of the teachings of Maj. Maj teaches treating depression comprising administering pramipexole (useful for treating Parkinson's disease) and sertraline. Rotigotine, the elected species is known in the art to treat

Parkinson's disease (Lauterbach). One having ordinary skill in the art would have been motivated to use rotigotine for another drug (pramipexole) used in Parkinson's disease in combination with sertraline in treating depression because of expectation of therapeutic benefits, synergistic or additive effects. It would have been obvious to one having ordinary skill in the art at the time of the invention to have administered one of the additional active ingredients in separate dosage forms by the same or different routes at the same or different times because of Maj's teachings. Maj teaches that in treating depression with sertraline the agents can be co-administered separately or as components of a single pharmaceutical dosage form and the drugs can be in different dosage forms. Also, administering another anti-depressant would be obvious because both compounds would be used to treat depression. "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose ....[T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). See also In re Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960); Ex parte Quadranti, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992); and In re Geiger, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987). Also, it is well within the skilled medical professional to determine suitable dosing regimens. It would have been customary for an artisan of ordinary skill to determine the optimal dosage of the drug in order to best achieve the desired results. Thus, absent some demonstration of

unexpected results from the claimed parameters, this optimization of route of delivery, dosage regimens would have been obvious at the time of applicant's invention.

Claim 58 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nichols et al. (U.S. 4,501,890) in view of Pfeiffer (Drugs Aging, 2002, vol. 19, no. 8, p. 561-570) and (Lauterback et al. (U.S. 2003/0027793) as applied to claims 10-15, 17, 30, 32-44 above and in view of Marquis (U.S. 6,350,773) and Timmerman (chapter 9, E J of pharmacology, 181, 1989, 253-60).

Nichols et al. in view of Pfeiffer and Lauterbach et al. teachings discussed as above.

The references do not teach addition of one or more antipsychotics to compound of formula of claim 17 in treating depression.

Marquis teaches a method and composition for the treatment of depression comprising the combination of a D2/D3 agonist and an antipsychotic such as thioridazine (i.e. an anxiolytic), fluphenazine, clozapine, haloperidol, thioridazine, risperidone and olanzapine (see column 1, lines 13-20; claims 3, 6 and 10). The combination can be in a unitary form or separately for simultaneous, separate or sequential administration (see paragraph 4, lines 1-8 and lines 55-63).

It would have been obvious to one having ordinary skill in the art to treat depression comprising administering compound of formula of claim 17, such as rotigotine (elected species) along with an antipsychotic agent, clozapine (elected species) in treating depression because of the teachings of Marquis. Marquis teaches treating depressive disorder comprising administering anti-psychotic agents including

clozapine and D2/D3 agonist. One having ordinary skill in the art would have been motivated to use rotigotine in combination with an anti-psychotic drug such as clozapine because clozapine has been shown to be useful in combination anti-depressant therapy. A person of ordinary skill in the art at the time of the invention would have been motivated to use ritogotine (another D2 agonist) for another D2 agonist along with clozapine in treating depression in expectation of similar or better therapeutic benefits. Also, Timmerman (chapter 9, E J of pharmacology, 181, 1989, 253-60) teaches N-0437 (rotigotine) as an antipsychotic drug. One having ordinary skill in the art would have been motivated to administer one anti-psychotic drug (rotigotine) for clozapine in Marquis's method of treating psychotic depression treatment in expectation of similar and or better therapeutic benefits of treating depression.

Claim 58 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nichols et al. (U.S. 4,501,890) in view of Pfeiffer (Drugs Aging, 2002, vol. 19, no. 8, p. 561-570) and (Lauterback et al. (U.S. 2003/0027793) as applied to claims 10-15, 17, 30, 32-44 above and in view of Hrdlicka (Eur Psychiatry, 2002, 17) and Timmerman (chapter 9, E J of pharmacology, 181, 1989, 253-60).

Nichols et al. in view of Pfeiffer and Lauterbach et al. teachings discussed as above.

The references do not teach addition of one or more antipsychotics to compound of formula of claim 17 in treating depression.

Hrdlicka teaches combination of clozapine and maprotiline (a tricyclic antidepressant) in refractory psychotic depression treatment. The reference teaches

that clozapine is antipsychotic agent and when administered along with maprotoline to a patient with recurrent depressive disorder.

It would have been obvious to one having ordinary skill in the art to treat depression comprising administering compound of formula of claim 17, such as rotigotine (elected species) along with an antipsychotic agent, clozapine (elected species) in treating depression because of the teachings of Hrdlicka. Hrdlicka teaches treating depressive disorder comprising administering clozapine and maprotiline (a tricyclic antidepressant). One having ordinary skill in the art would have been motivated to use rotigotine in combination with an anti-psychotic drug such as clozapine because clozapine has been shown to be useful in combination anti-depressant therapy. A person of ordinary skill in the art at the time of the invention would have been motivated to use ritogotine along with clozapine in treating depression in expectation of similar or better therapeutic benefits as obtained with clozapine in treating depression. Also, Timmerman (chapter 9, E J of pharmacology, 181, 1989, 253-60) teaches N-0437 (rotigotine) as an antipsychotic drug. One having ordinary skill in the art would have been motivated to administer one anti-psychotic drug (rotigotine) for clozapine in Hrdlicka's method of treating psychotic depression treatment in expectation of similar and or better therapeutic benefits of treating depression.

Claim 60 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nichols et al. (U.S. 4,501,890) in view of Pfeiffer (Drugs Aging, 2002, vol. 19, no. 8, p. 561-570) and (Lauterback et al. (U.S. 2003/0027793) as applied to claims 10-15, 17, 30, 32-44 above and in view of Rimpler et al. (US 2003/0180332 A1).

Nichols et al. in view of Pfeiffer and Lauterbach et al. teachings discussed as above.

The references do not teach addition of one or more sedatives to compound of formula of claim 17 in treating depression.

Rimpler et al. teach that rotigotine (N-0923) and its metabolites and prodrugs can be administered with other agents such as diphenhydramine (see paragraphs 89, 110 and 119).

It would have been obvious to one having ordinary skill in the art to treat depression comprising administering compounds of formula of claim 17, such as rotigotine along with a sedative agent, such as diphenhydramine (elected species) in combination therapy of treating depression because Rimpler teaches rotigotine can be administered with other agents including diphenhydramine. One having ordinary skill in the art would have been motivated to use a sedative agent such as diphenhydramine along with an antidepressant in combination therapy in treating depressive patients is to help the patients and improve the quality of sleep in the patients.

Claim 60 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nichols et al. (U.S. 4,501,890) in view of Pfeiffer (Drugs Aging, 2002, vol. 19, no. 8, p. 561-570) and (Lauterback et al. (U.S. 2003/0027793) as applied to claims 10-15, 17, 30, 32-44 above and in view of Kupfer (Ann Clin Psychiatry, 1999, 11(4), 267-76) and Cook et al. (2002/0177626).

Nichols et al. in view of Pfeiffer and Lauterbach et al. teachings discussed as above.

The references do not teach addition of one or more sedatives in treating depression.

Kupfer teaches that depressed patients often report problems sleeping and epidemiologic evidence suggests that insomnia may precede the onset of depression (see Abstract).

It would have been obvious to one having ordinary skill in the art to treat depression comprising administering compounds of formula of claim 17, such as rotigotine along with a sedative agent, such as diphenhydramine (elected species) in combination therapy of treating depression because of the teachings of Kupfer. Kupfer teaches that depressed patients often report problems sleeping and it is known in the art that diphenhydramine is a sedative (US 20020177626). One having ordinary skill in the art would have been motivated to use a sedative agent along with an antidepressant in combination therapy in treating depressive patients is to help the patients and improve the quality of sleep in the patients.

Claim 62 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nichols et al. (U.S. 4,501,890) in view of Pfeiffer (Drugs Aging, 2002, vol. 19, no. 8, p. 561-570) and (Lauterback et al. (U.S. 2003/0027793) as applied to claims 10-15, 17, 30, 32-44 above and in view of Zimmerman et al. (Am J Psychiatry 160:504-512, March 2003) and (Lehmann, *Neuropsychobiology* 1989;21:197-204, Abstract)

Nichols et al. in view of Pfeiffer and Lauterbach et al. teachings discussed as above.

The references do not teach addition of one or more anxiolytics in treating depression.

Zimmerman teaches that compared to the depressed patients without generalized anxiety disorder, the depressed patients with modified generalized anxiety disorder had higher levels of suicidal ideation; poorer social functioning; a greater frequency of other anxiety disorders, eating disorders, and somatoform disorders (See abstract).

It would have been obvious to one having ordinary skill in the art to treat depression comprising administering compounds of formula of claim 17, such as rotigotine along with an anxiolytic agent, such as fluspirilene in combination therapy of treating depression because the prior art teachings teach that the depressed patients with modified generalized anxiety disorder had higher levels of suicidal ideation; poorer social functioning; a greater frequency of other anxiety disorders, eating disorders, and somatoform disorders. Fluspirilene is known in the art as an anxiolytic agent (Lehmann, *Neuropsychobiology* 1989;21:197-204, Abstract). One having ordinary skill in the art would have been motivated to use an anxiolytic agent along with an antidepressant in combination therapy in treating depressive patients to provide therapeutic benefits for anxiety disorder.

Claim 64 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nichols et al. (U.S. 4,501,890) in view of Pfeiffer (Drugs Aging, 2002, vol. 19, no. 8, p. 561-570) and (Lauterback et al. (U.S. 2003/0027793) as applied to claims 10-15, 17, 30, 32-44

above and in view of document, Links between Depression and Migraine (5/19/2003) and Livingstone et al. (US 2003/0225002).

Nichols et al. in view of Pfeiffer and Lauterbach et al. teachings discussed as above.

The references do not teach addition of one or more anti-migraine in treating depression.

Links between Depression and Migraine document teaches that risk of migraine in individuals with pre-existing major depression was three times higher than in individuals with no history of depression and the risk of major depression in persons with pre-existing migraine was more than fivefold higher than in people with no history of headaches.

It would have been obvious to one having ordinary skill in the art to treat depression comprising administering compounds of formula of claim 17, such as rotigotine along with an anti-migraine agent, such as almoptriptan in combination therapy of treating depression because the prior art teachings teach the connection between migraine and depression. Almotriptan is known in the prior art as an anti-migraine agent (US 20030225002). The document Links between Depression and Migraine teaches that patients with depression had higher risk of migraine. One having ordinary skill in the art would have been motivated to use an anti-migraine agent along with an antidepressant in combination therapy in treating depressive patients to provide therapeutic benefits for migraine.

## Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to UMA RAMACHANDRAN whose telephone number is (571)272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shengjun Wang/
Primary Examiner, Art Unit 1627

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